Case Report

Fuchs Heterochromic Iridocyclitis: A Complex Disease Process

V502 Problem Based Learning

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A thirty-five-year-old white female patient presented for a comprehensive eye exam with no visual complaint or ocular history. The review of systems is unremarkable with no current medications or allergies. Her visual acuities are 20/20 OU. Upon examination in daylight conditions, her irises were slightly different colors. The patient reports that she has always had blue eyes, but now OD appears browner than OS. With the slit lamp, indications of active inflammation are observed in the patient’s OD. Specifically, some cells and flare were observed in the anterior chamber (AC), and keratic precipitates were observed on the posterior cornea. The cells are white blood cells visible in the AC, and the flare is protein leaking into the normally-clear aqueous. In conjunction, these symptoms are classic for a low-level uveitis. Lastly, evaluation of the lens revealed a posterior subcapsular cataract. Intraocular pressures (IOPs) were assessed with Goldman tonometry at 22 mmHg OD/16 mmHg OS. The patient was recommended for follow-up dilated fundus exam (DFE).

The iris is a relatively thin colored structure which lies in front of the lens in the anterior chamber of the eye. The iris is part of the uveal tunic of the eye, which also comprises the ciliary body and choroid. Relevantly, this intermediate layer is also referred to as the vascular tunic. The thin structure of the iris contains two smooth muscles composed of neuroectoderm: the radial and the sphincter muscles. These muscles form an antagonist pair which expands and constricts to control the diameter of the pupil. This mechanism allows autonomic innervation to signal in agreement with the pupillary light reflex, arousal, acute stress, attention level and the near triad.

Regulation of retinal illumination is accomplished by the dynamic size of the pupillary aperture. A mitotic or small pupil is produced by parasympathetic stimulation of the sphincter. Conversely, stimulation of the dilator muscle via sympathetic fibers causes a mydriatic or large pupil. In a bright setting, the normal pupil diameter averages from two to four mm. Typically, in a dark environment, the pupil diameter is four to eight mm. The pupil sizes, direct responses and consensual responses are always assessed during an eye exam as they are a significant sign of the health of the nerve pathways. Typically, pupils are equal, round, and reactive to light with accommodation, commonly condensed to PERRLA. If the pupils are not symmetrical in size, known as anisocoria. Asymmetric pupils, or abnormal stimulus responses, in the dark can be indicative of relative afferent pupil defect (RAPD) or Marcus Gunn pupil. An RAPD is indicative of a lesion in the optic nerve anterior to the optic chiasm.

The iris, aptly named after the Greek goddess of the rainbow, is often vividly pigmented and variegated. Melanocytes are cells within the iris layers that produce melanin, a pigment which blocks light and reduces scatter. The concentration of this pigment in the anterior border and stromal layers of the iris is chiefly responsible for the numerous color hues and intricate patterns. Regular topographical features of the iris include contraction furrows, Fuchs' crypts, nevi, a corona and a pupillary ruff. The average iris diameter is approximately twelve mm, and the normal circumference is thirty-seven mm. The middle of the iris is also the thickest area, marked by a circular fringe structure known as the collarette. The thinnest area is the iris root located at the periphery, where the iris is anchored to the ciliary body. This region in the AC is identified as the iridocorneal or drainage angle. The thin iris root can tear away from the angle, known as iridodialysis, as a result of blunt trauma or intraocular surgery.
Heterochromia iridis is the abnormal, but not uncommon, condition of different colored irises on the same person.\textsuperscript{20} The altered coloration can be sectorial, central, segmental or complete.\textsuperscript{21} Heterochromia affects fewer than two-hundred-thousand individuals in the United States. Heterochromia is not usually indicative of disease as most cases are harmless and intermittent. Notwithstanding, the causes of heterochromia can be congenital or acquired through a drug side effect, inflammatory disease process or trauma. Congenital heterochromia is present in several syndromes including, Horner’s, Waardenburg, and Parry–Romberg.\textsuperscript{22} The differential diagnosis for this patient’s acquired heterochromia with subdued uveitis include Fuchs’ Heterochromic Iridocyclitis (FHI), tumors, trauma, rubeotic iridis, long-standing hyphema, or a pharmacological side effect. FHI is the first to investigate due to acquired heterochromia and the characteristic triad of inflammatory markers, cataract formation, and elevated asymmetric IOPs.\textsuperscript{23,24}

The patient returned to the clinic for a follow-up DFE a few days after the initial exam. Posterior pole examination reviewed normal findings for the retina, macula, and optic nerve. The C/D ratios were 0.2 OU with rim tissue healthy. The optic nerve findings are essential because ocular hypertension has not yet manifested in glaucomatous damage.\textsuperscript{25,26} The right eye contained trace deposits in the anterior vitreous and none in the fellow eye. The presence of subtle vitreous cells and debris continues to support the tentative diagnosis of subdued uveitis of the right eye related to FHI.\textsuperscript{27,28} The IOPs were remeasured 26 mmHg OD/18 mmHg OS, slightly higher in both eyes. The iridocorneal angle was evaluated using indirect gonioscopy because the status of the angle is of great consequence to glaucoma etiology.\textsuperscript{29}

Gonioscopy is an indispensable exam procedure used to view the anterior chamber and drainage angle. This technique overcomes total internal reflection with a goniolens placed directly on the cornea with lubricating fluid. First, the procedure is briefly explained to the patient and the room darkened. Next, the lens is sanitized, and a viscoelastic gel is applied to the lens-cornea interface. Then, the patient’s cornea is anesthetized using a topical agent, and the slit lamp is prepared for observation. The patient’s eyelids are gradually opened as the lens is directed on top of the anterior ocular surface. Interpretation of the angle is made while maintaining the slit lamp focus. The goniolens is then gently rotated to view each section of the angle. Finally, the lens is removed by using the eyelids to break the suction of the lens-cornea interface.\textsuperscript{30,31}

William van Herick, an American ophthalmologist, developed a time-honored internationally recognized four-point grading system in 1969.\textsuperscript{32} A slit lamp is used to create a thin optic section of light at an angle of sixty degrees to estimate chamber depth. Using this light, the doctor illuminates the nasal or temporal angle as near the limbus as possible. The depth of the corneal section illuminated is compared directly to the width of the ‘black space’ found between the area of the iris illuminated. For example, in a Grade 4 wide-open angle the black space is equal to or greater than the corneal band illuminated.\textsuperscript{33,34}

Furthermore, systematically interpreting, grading and communicating the gonioscopic images is the topic of a significant amount of research. Scheie and Schaffer are prevalent systems which also use a five-point scale. In Scheie’s spectrum, the scale is inverted, zero is a cavernous angle and IV represents closed with no angle structures visible. Similar to van Herick’s, on the Schaffer scale, Grade 4 is open with the ciliary body visible, and grade 0 signifies closed. Spaeth
developed a scale which is much more esoteric and contains more descriptors on insertions, configurations and pigmentation level.  

During gonioscopy of the right eye, fine rubeotic vessels were seen in the patient’s ciliary body and trabecular meshwork. Nonetheless, the patient’s angle was open with no signs of peripheral synechia. If the arborizing vessels that are crossing into the trabecular meshwork create hyphema, it is known as Amsler’s sign. The neovascular vessels residing in the angle are vulnerable to rupture during intraocular surgery. If rupture occurs, cytokines released from the bloodstream can further augment inflammation and advance tissue proliferation which can lead to neovascular glaucoma, a much more devastating disease.

A synechia is when the iris is adhering to a dissimilar surface. There are two general types of synechiae, peripheral and posterior. A peripheral anterior synechia (PAS) is a disorder in which the iris clings to the iridocorneal angle, obstructing aqueous outflow. For this patient, lack of a PAS is a good sign that the drainage apparatus appears open. A posterior synechia is a condition in which a segment of the iris fastens itself to the crystalline lens. A ring or annular synechia is adhesion of the entire circumference of the pupil to the anterior capsule of the lens. This causes the aqueous to become restricted to the posterior chamber. An iris bombe is a classic appearance of the iris when there is a ring synechia, characteristically the iris bows into the anterior chamber from the aqueous humor pressure accumulation.

Cataracts, a clouding of the crystalline lens, are cataloged via location, grade of opaqueness, maturity or by the underlying stimulus. The re-examination of the patient again revealed posterior subcapsular cataract (PSC). This type of cataract involves the migration and deposition of equatorial epithelial cells into the normally clear collagenous posterior capsule of the lens. PSCs tend to affect vision rather quickly, so one can assume this cataract is fairly immature because the patient’s visual acuity was 20/20 OU, worsening to 20/40 OD. The etiologies of PSCs are multifactorial: age of the patient, hyperglycemia, long-term glucocorticoid use, anterior inflammation, or radiation exposure.

The signs and symptoms continue to confirm the tentative diagnosis of Fuchs’ Heterochromic Iridocyclitis with secondary glaucoma. In 1843, the pattern of heterochromia and associated cataract was first remarked by Sir William Lawrence. Later, Ernst Fuchs’, an Austrian ophthalmologist, effectively outlined the condition in 1906. Fuchs’ *Textbook of Ophthalmology* was deemed the bible of ophthalmology for many years. As a result, Fuchs’ name accompanies many anterior segment disorders and anatomical features. A typical FHI patient is 20-40 years old, with mild or no complaints and is customarily unilateral. Nevertheless, FHI has comorbidities that combine to make it a syndrome: acquired iris heterochromia, a low-grade chronic inflammatory progression, and widely scattered uniform keratic precipitates. Stereotypical complications include a cataract, commonly PSC, and occasionally glaucoma, secondary to the inflammation. Crucially, FHI has no minimal clinical diagnostic criteria, consequently the diagnosis much be reached by exclusion.

Glaucoma is a diverse group of diseases, analogous to cancer that is also a group of diseases, which destroy the eye’s neural tissue. The World Health Organization estimates glaucoma to be the a leading cause of blindness worldwide, second only to cataract. Glaucomatous damage is
often referred to as the sneak thief of sight because it is insidiously asymptomatic, traditionally beginning by slowly affecting the peripheral aspects of the visual field. If left untreated, the damage is slow but persistently progressive to blindness. This is compounded by the fact that glaucoma associated with FHI is frequently uncooperative to drug therapy. Due to the sinister nature of the patient’s ocular hypertension, Alphagan, brimonidine tartrate ophthalmic solution, was prescribed twice a day in the right eye. Alphagan is an extremely selective alpha-2 adrenergic agonist, which reduces cyclic adenosine monophosphate (cAMP) and the site of action is the ciliary body epithelial cells. Alphagan is frequently prescribed to reduce IOPs by effectively reducing aqueous humor production and potentially provides a synergistic benefit by also increasing uveoscleral outflow as the ciliary body undergoes vasoconstriction.

In this case, Alphagan was preferred over a prostaglandin analog, such as latanoprost, because prostaglandins have been shown to excite the inflammatory response. With more conventional cases of uveitis, high-potency prednisolone is the conventional first course to rein in inflammation. On the other hand, the doctor should be suspicious of FHI if the patient is twenty to forty years old and possesses heterochromia, keratic precipitates, and low-lying anterior uveitis. A red flag should rise if the uveitis becomes worse with the heavy-hitting prednisolone regimen. Prognosis for those with FHI is favorable with proper compliance, frugal corticosteroid use, and eventual successful cataract surgery.
References


